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Is cognitive behavioral therapy (CBT) effective in reducing depressive and manic symptoms in people with bipolar disorder when compared to treatment as usual (TAU)?

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Is cognitive behavioral therapy (CBT) effective in reducing depressive and manic symptoms in people with bipolar disorder when compared to treatment as usual (TAU)?

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A SELECTIVE EVIDENCE BASED MEDICINE REVIEW

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ABSTRCT

OBJECTIVE: The objective of this selective EBM review is to determine whether or not cognitive behavioral therapy (CBT) is effective in reducing depressive and manic symptoms in people with bipolar disorder when compared to TAU.

STUDY DESIGN: Systematic review of three randomized controlled trials published in 2011, 2012, and 2014.

DATA SOURCES: Data sources for this review were articles published in peer-reviewed journals using PubMed and Cochrane Collaboration.

OUTCOME(S) MEASURED: The outcomes measured were a decrease in depressive and manic symptoms through the use of rating scales.

RESULTS: Costa et al. (2011) showed a greater decrease in depressive and manic symptoms with cognitive behavioral therapy than with treatment as usual ($p<0.01$). West et al. showed a reduction in depressive ($p<0.007$) and manic ($p<0.03$) symptoms with CBT compared to the control group receiving general psychotherapy as well as a NNT of 2 for mania. Finally, Costa et al. (2012) showed a greater decrease in depressive and manic symptoms with CBT than TAU ($p<0.01$). In total, each study showed a greater reduction in depressive than manic symptoms.

CONCLUSIONS: All studies evaluated in this EBM review showed that CBT is effective at reducing depressive and manic symptoms associated with bipolar disorder. Major limitations of the study were the sample sizes and the fact none of the participants included had severe depressive or manic symptoms. Further studies are needed to conclude that CBT is effective for bipolar disorder.

KEY WORDS: Bipolar disorder, Cognitive behavioral therapy

INTRODUCTION

Bipolar disorder is a chronic or episodic mental disorder that can cause unusual, often extreme and fluctuating changes in mood, energy, activity, and concentration or focus.[1] Bipolar disorder affects approximately 2.8% (estimated 7 million people) adult Americans per year in the United States.[2] An exact number for the total healthcare cost of all three types of bipolar disorder has not been identified. It is estimated that in 2015, $202.1 billion (averaging to $81,559 per individual) was spent for bipolar disorder I.[3] There is no current information on the number of healthcare visits per year but between 2002-2003 there had been 1,003 visits per 100,000 population.[4] Due to the growing recognition of mental health disorders, bipolar disorder is not uncommon to see across any specialty.

The exact cause of bipolar disorder is unknown. However, research suggests that a combination of factors contribute to bipolar disorder including stress, genes, and brain structure and function.[1] There are three types of bipolar disorder: bipolar I, bipolar II, and cyclothymic. Each type involves a change in mood, energy, and activity level alternating with a normal (euthymic) mood.[1] Suicide is the number one cause of premature death among people with bipolar disorder.[5]

While there is no curative treatment for bipolar disorder, there are several pharmacologic and non-pharmacologic methods that are used to control and maintain the depressive and manic symptoms that are associated. Pharmacologic treatments include mood stabilizers (i.e. lithium, valproic acid, and lamotrigine), antidepressants (i.e. bupropion, fluoxetine, and sertraline), and anxiolytics (i.e. lorazepam and clonazepam). Psychotherapy may include CBT, family therapy, interpersonal therapy, and psychoeducation. For severe or refractory cases, electroconvulsive therapy (ECT) may be used. Other non-pharmacological methods target lifestyle management

including regular vigorous exercise (i.e., jogging, swimming, and biking) and keeping a life chart with daily mood, treatments, sleep patterns, and life events.

The treatment options mentioned above all play an effective role in treating bipolar disorder. However, with medications being a primary treatment, patients respond and tolerate each differently. The use of medications also carries out the risks of various side effects and potentially serious adverse reactions. In addition, the use of medications for a long period of time may lead to tolerance and eventual drug resistance which further increases the risk of relapses. While the use of medications may carry risks, the use of CBT has been shown to be effective in reducing depression and mania associated with bipolar disorder and does not have serious side effects like current treatments. Individual studies have shown CBT to be an effective method of treatment for bipolar disorder, but a comprehensive analysis has not been done. This paper evaluates three randomized controlled trials comparing the efficacy of cognitive behavioral therapy (CBT) in reducing depressive and manic symptoms in people with bipolar disorder with treatment as usual (TAU).

OBJECTIVE

The objective of this EBM review is to determine whether or not cognitive behavioral therapy is effective in reducing depressive and manic symptoms in people with bipolar disorder when compared to TAU. Hypothesis about the objective is that the use of CBT is effective in reducing depressive and manic symptoms in people with bipolar disorder when compared to TAU.

METHODS

The criteria used included the population, interventions, comparisons, outcomes measured, and the types of studies included. The population included people, both male and

female, with bipolar disorder. The intervention used was cognitive behavioral therapy (CBT). The comparison used was treatment as usual (TAU) which includes both medications and psychotherapy. The outcomes measured was the efficacy of CBT for the treatment of depression and mania associated with bipolar disorder based on various rating scales given and evaluated by the investigator. The studies included in this EBM review include three randomized controlled trials.

PubMed and Cochrane Collaboration were used in order to find the articles used for this systematic review. Articles were selected based on their relevance to the clinical question and if the outcomes of the study mattered to the patients. All articles were published in peer-reviewed journals within the past 10 years. The key words “bipolar disorder” and “cognitive behavioral therapy” were used to search for the articles. All articles were published in English. The inclusion criteria included articles that were randomized controlled trials, full text, published in the last 10 years, English, and Child: birth-18 years. Exclusion criteria included studies that were published before 2010. Table 1 further discusses inclusion and exclusion criteria from each study. Statistics were reported using mean change from baseline, p-values, and NNT.

OUTCOMES MEASURED

The outcomes measured in Costa et al. (2011) and Costa et al. (2012) studied the patient perception of reduction in depressive and manic symptoms based on the total severity of the self-reported rating scales, Beck Depression Inventory (BDI) and Young Mania Rating Scale (YMRS). The BDI has 21 questions with ratings between 0-3. The patient fills out the questionnaire and then the total score is added up and then correlated with a level of depression. The YMRS has 11 questions with ratings between 0-4 with the same procedure as the BDI. The outcomes measured in West et al. studied the parent perception of reduction in depressive and

manic symptoms in pediatric patients based on the total severity of the rating scales, Child Bipolar Depression Rating Scale (CBDRS) and Child Mania Rating Scale (CMRS). The CMRS has 21 questions with the rating between 0-3, that is filled out by the parent, and the total score is added up and compared to a mania scale determining the severity. The CBDRS is similar to CMRS but measures the level of depression. For each rating scale, a higher score indicates more severe disease. The study conducted by West et al. focused specifically on children while the other two studies focused on patients 18 years and older. In all three studies, the CBT group was compared to the TAU group.

RESULTS

In the study conducted by Costa et al. (2011), 41 subjects were recruited from an Anxiety and Depression Program Outpatient Clinic in Rio de Janeiro. Subjects were studied over a period of 14 weeks while receiving CBT for depressive and manic symptoms related to bipolar disorder.[6] Each subject in the CBT group attended two-hour sessions per week prescribed by an experienced clinical psychologist trained in CBT.[6] Each subject in the control group attended sessions prescribed by their psychiatrists.[6]

The BDI for the CBT group showed a decrease in symptom score by an average of 12.28 which correlates with an improvement in depressive symptoms. The BDI for the control group showed an increase in symptom score by an average of -2.25 which correlates with no improvement or worsening depression.

The YMRS for the CBT group showed a decrease in symptoms score by an average of 7.44 which correlated with an improvement in manic symptoms. The YMRS for the control group showed an increase in symptom score by an average of -1.59 which correlates with no improvement or worsening mania.

Table 1. Demographics & Characteristics of Included Studies

Study	Type	# Pts	Age (yrs)	Inclusion Criteria	Exclusion Criteria	W/D	Interventions
Costa[6] (2011)	RCT	41	18-60	-Met DSM-IV criteria for BD I or II and experienced at least one hypomanic, manic or depressive episode in previous 12 months -Euthymic, mildly depressed or mildly hypomanic at the time of initial assessment	BDI score >34 and a YMRS >20 or presented a comorbid personality d/o and/or other axis I severe psych d/o	4	TAU attended sessions prescribed by psychiatrist, no psychotherapy VS. 14 cognitive behavioral group therapy sessions divided into two stages, 2 hours each
West[7] (2014)	RCT	69	7-13	Stabilized on medication, parental consent, youth assent	Youth IQ <70, active psychosis, active substance abuse/ dependence, neurological or other medical problems that complicate psych symptoms, active suicidality resulting in hospitalization	22	Each group: 12 weekly sessions and 6 monthly follow up sessions Untrained in CFF-CBT VS. Trained in CFF-CBT
Costa[8] (2012)	RCT	41	18-55	Men and women aged 18-60 who met DSM-IV for BD I or II and experienced at least one hypomanic, manic or depressive episode in previous 12 months	BDI >35 and/or YMRS >20, comorbid personality d/o and/or other axis I severe psych d/o; substance abuse/ dependence; severe psychical illness; new mood stabilizer or antidepressant	4	Therapy sessions prescribed by psychiatrist VS. 14 group cognitive behavioral therapy weekly sessions, 2 hours each, 2 phases

The authors found that this greater decrease of depressive and manic symptoms with CBT was statistically significant at $p<0.01$.[6] The study reports that the data was analyzed using the Pearson chi-square tests, ANOVA, paired-sample t-test, and a multiple regression analysis.[6] They reported that CBT was well tolerated by most of the subjects with only one subject from the CBT group requiring hospitalization for reasons not discussed.[6]

Table 2. Mean (SD) BDI changes at 7 Weeks and 14 Weeks from Baseline in Costa et al. 2011

	Baseline: Mean (SD)	**Week 7: Mean (SD)**	**Week 14: Mean (SD)**	**Mean change from baseline**
CBT group	19.52 (9.79)	12.00 (7.90)	7.24 (6.42)	12.28, p <0.01
Control group	11.67 (8.39)	12.58 (8.36)	13.92 (9.17)	-2.25, p <0.01

Table 3. Mean (SD) YMRS Changes at 7 Weeks and 14 Weeks from Baseline in Costa et al. 2011

	Baseline: Mean (SD)	**Week 7: Mean (SD)**	**Week 14: Mean (SD)**	**Mean change from baseline**
CBT group	9.68 (8.03)	6.72 (6.20)	2.24 (3.22)	7.44, p <0.01
Control group	1.33 (3.37)	3.17 (3.16)	2.92 (2.81)	-1.59, p <0.01

In the study conducted by West et al., 69 pediatric subjects were recruited from a specialty pediatric mood disorders clinic in an urban academic medical center. The subjects were randomly assigned to either the CBT group or control group and received treatment for a total of eight weeks.[7] The CBT group received weekly CBT and the control group received general psychotherapy with therapists who were not trained in CBT.[7] In addition, the authors of this study included families in the therapy sessions to help engage the children and help them retain the information being taught.[7] CBDRS and CMRS were performed by their parents at baseline, weeks 4 and 8 (during treatment), week 12 (post-treatment), and week 39 (follow-up).[7]

The CBDRS in the CBT group showed improvement with an average change of 9 from baseline to follow-up at week 39 while the control group only showed an average change of 4 over the same time period. The larger average change in symptom score of CBDRS in the CBT

group indicates that CBT helped with depressive symptoms more than the control group. The authors found that this decrease in symptoms with CBT was statistically significant at $p<0.007$.[7]

The CMRS in the CBT group showed improvement with an average change of 6 from baseline to follow-up at week 39 while the control group only showed an average change of 2 over the same time period. The larger average change in symptom score of CMRS in the CBT group indicates that CBT helped with manic symptoms more than the control group. The authors found that this decrease in symptoms with CBT was statistically significant at $p<0.03$.[7] In addition, a numbers needed to treat (NNT) of 2 was calculated. This NNT signifies that two subjects would need to be treated with CBT for one more subject to see a positive effect compared to the control group.

The study reports that mixed-effects regression models (MRM's) were conducted via SPSS MIXED to examine the responses of each outcome.[7] The authors also included the intent to treat analysis indicating that all subjects that were initially enrolled in the study and randomized to a group were included in the analysis.[7]

Table 4. Average CBDRS Symptom Scores at Weeks 4, 8, 12, and 39 from Baseline in West et al.

	Baseline	**Treatment Week 4**	**Treatment Week 8**	**Post-treatment Week 12**	**Follow-up Week 39**	**Change from baseline**
CBT group	20	18	15	14	11	9, $p<0.03$
Control group	27	27	24	27	23	4, $p<0.03$

Table 5. Average CMRS Symptom Scores at Weeks 4, 8, 12, and 39 from Baseline in West et al.

	Baseline	**Treatment Week 4**	**Treatment Week 8**	**Post-treatment Week 12**	**Follow-up Week 39**	**Change from baseline**
CBT group	18	18	13	13	12	6, $p<0.007$
Control group	20	19	21	19	18	2, $p<0.007$

Table 6. NNT for CMRS Calculated Based on the CBT Group and Control Group at Post-treatment

CER	EER	RBI	ABI	NNT
0.21	0.88	3.19	0.67	2

In the study conducted by Costa et al. (2012), 41 subjects were recruited from the Institute of Psychiatry of the Federal University of Rio de Janeiro. The subjects were evaluated over a 14-week period while receiving either CBT prescribed by an experienced clinical psychologist trained in CBT or TAU.[8] Each subject in the CBT group attended weekly sessions lasting two-hours each and focused on educating the patient about their condition and the treatment process, teaching them methods for monitoring their symptoms and staying compliant with treatment, and providing them with strategies to cope and manage with stress that ultimately may lead to worsening symptoms.[8] Each subject in the control group attended regular therapy sessions prescribed by the psychiatrist.[8]

The BDI for the CBT group showed an average change of 12.28 at week 14 which indicates that the depressive symptoms improved with treatment. The BDI for the control group showed an average change of -2.25 at week 14 which indicates that the depressive symptoms remained the same or worsened with treatment.

The YMRS for the CBT group showed an average change of 7.44 at week 14 which indicates that the manic symptoms improved with treatment. The YMRS for the control group showed an average change of -1.59 at week 14 which indicates that the manic symptoms remained the same or worsened with treatment.

The authors found that this greater decrease of depressive and manic symptoms with CBT was statistically significant at $p<0.01$.[8] NNT was not calculated for this study because the data were not dichotomous. The study reports the data were analyzed using Pearson chi-square,

Fisher exact tests, statistical analysis of variance, and regression analysis.[8] The authors reported that CBT was well tolerated and only one subject required hospitalization for reasons not discussed.

Table 7. Mean ± SD BDI Changes at 7 Weeks and 14 Weeks from Baseline in Costa et al. 2012

	Baseline: Mean ± SD	**Week 7: Mean ± SD**	**Week 14: Mean ± SD**	**Mean change from baseline**
CBT group	19.52 ± 9.79	12.00 ± 7.90	7.24 ± 6.42	12.28, p <0.01
TAU group	11.67 ± 8.39	12.58 ± 8.36	13.92 ± 9.17	-2.25, p <0.01

Table 8. Mean ± SD YMRS Changes at 7 Weeks and 14 Weeks from Baseline in Costa et al. 2012

	Baseline: Mean ± SD	**Week 7: Mean ± SD**	**Week 14: Mean ± SD**	**Mean change from baseline**
CBT group	9.68 ± 8.03	6.72 ± 6.20	2.24 ± 3.22	7.44, p <0.01
TAU group	1.33 ± 3.37	3.17 ± 3.16	2.92 ± 2.81	-1.59, p <0.01

DISCUSSION

Bipolar disorder is a lifelong condition that can negatively impact the quality of life especially in populations that don't have access to proper medical care. Unfortunately, suicide is common among those with the disorder. Because bipolar disorder usually requires medical treatment with a combination of pharmacotherapy, psychotherapy, and lifestyle approaches, compliance often becomes a concern. Medications can be expensive and usually require weeks to months to build in the system and produce notable effects. In addition, everybody responds to medications differently and it may take a few medications before finding the one that works best. Many medications produce undesirable side effects that may lead patients to stop. Attending psychotherapy can be challenging due to cost, location, access, and timing. Due to these concerns, many with bipolar disorder get treated as an inpatient until they learn and are comfortable managing the depressive and manic symptoms on their own.

The three trials that were discussed within this EBM review indicate that CBT can be effective in reducing depressive and manic symptoms in people with bipolar disorder. In the studies by Costa et al. (2011) and Costa et al. (2012), both the BDI and YMRS results showed a statistically significant reduction in depressive and manic symptoms over a 14-week period. In the study by West et al., both the CBDRS and CMRS showed a reduction in depressive and manic symptoms from baseline to follow-up at 39 weeks. In addition, most of the subjects throughout each study were able to tolerate CBT with a couple subjects hospitalized for reasons not discussed. Tolerability is another benefit of CBT when comparing it to pharmacotherapy because of the possible adverse reactions that medications may produce.

Although there were limitations among each of the studies, the authors felt that the studies ultimately proved that cognitive behavioral therapy is superior to treatment as usual whether that be pharmacotherapy, psychotherapy, or both. The biggest limitation among all of the studies was the number of participants included.[6,7,8] Although the studies by Costa et al. (2011) and Costa et al. (2012) had very few participants withdrawal, the study by West et al. had a large number of people withdrawal which weakens the strength of the study. In Costa et al. (2011) and Costa et al. (2012), the age groups ranged from young adult to middle aged which can create limitations because bipolar disorder presents differently with age. In addition, bipolar I, bipolar II, and cyclothymic disorder all present differently but the studies[6,7,8] did not specify which type the subjects had. In all three of the studies,[6,7,8] none of the participants included had severe depression and mania symptoms so it is unknown if CBT will produce a similar reduction in symptoms. Although double-blinding in CBT trials cannot be done, none of the studies[6,7,8] single-blinded the raters which impacts the validity because it can create bias. Because there are very few studies that focus on CBT for depressive and manic symptoms associated with bipolar

disorder, these studies produced clinically significant information that can help researchers determine a foundation for future studies and clinicians with managing their patients.

CONCLUSIONS

This systematic review provided insight into three studies that used cognitive behavioral therapy for the treatment of depressive and manic symptoms associated with bipolar disorder. Because all three studies showed clinically significant results, it was determined that cognitive behavioral therapy is effective at reducing depressive and manic symptoms when compared to treatment as usual which could include general psychotherapy, pharmacological treatment, or both. Mental health illnesses are becoming more recognized across all health care fields so various treatment options are being tested to determine efficacy and benefit. Although, there will never be one method listed as the gold standard for the treatment of any mental health condition, treatment should be approached with multiple methods. Each patient should be treated individually with a combination of pharmacological, psychotherapy (including CBT), and lifestyle changes. More research needs to be conducted on cognitive behavioral therapy to ultimately determine the efficacy of this treatment method especially compared to pharmacotherapy which is a major method of treatment. Future studies should focus on increasing the number of participants to help strengthen the study and ensure the data analyzed is more accurate. In addition, there should be focus on patients with severe mania and depression, different age groups, male versus female patients, and different socioeconomic classes to determine which groups benefit most from CBT. Researchers should also increase therapy sessions to multiple times per week especially in those with more severe bipolar symptoms. Bipolar disorder is a complex disorder and each patient should be treated with an individualized plan that is best tailored to their lifestyle.

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